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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/505,244

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Scott K. Kuwada

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Ballard Spahr LLP

SUITE 1000

999 PEACHTREE STREET

ATLANTA, GA 30309-3915

EXAMINER

PAGONAKIS, ANNA

ART UNIT

PAPER NUMBER

1628

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/505,244	Applicant(s) KUWADA, SCOTT K.	
	Examiner ANNA PAGONAKIS	Art Unit 1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 December 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,8-15,18,19,26-28,37-42,65,66 and 68-72 is/are pending in the application.
- 4a) Of the above claim(s) 19 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,8-15,18,26-28,37-40,42,65,66 and 68-72 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1 sheet; 12/24/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's payment and submission filed 12/24/2009, has been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's arguments filed 12/24/2009 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Status of Claims

Claims 1, 8-15, 18-19, 26-28, 37-42, 65-66 and 68-72 are currently pending.

Claims 19 and 41 remain withdrawn.

Claims 1, 8-15, 18, 26-28, 37-40, 42, 65-66 and 68-72 are currently under examination and the subject matter of the current Office Action.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8-15, 18, 26-28, 37-40, 42, 65-66 and 68-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification while enabling for the treatment of seeding HT-29 colon cancer cells

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prior to surgical resection with administration of BAY 11-7085, does not reasonable provide enablement for a method of inhibiting reseeding of cancer cells during or after surgical resection of a tumor comprising administering to a subject within 10 days of the resection a compound having the structure exemplified in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is mostly nearly connected, to make and use the invention in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

- 1) the nature of the invention;
- 2) the breadth of the claims;
- 3) the predictability or unpredictability of the art;
- 4) the amount of direction or guidance presented;
- 5) the presence or absence of working examples;
- 6) the quantity of experimentation necessary;
- 7) the state of the prior art; and,
- 8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The presently claimed invention is drawn to a method of inhibiting reseeding of cancer cells during or after surgical resection of a tumor comprising administering to a subject within 10 days of the resection a compound having the structure exemplified in claim 1.

The instant specification as originally filed lacks adequate guidance, direction or discussion to apprise the skilled artisan how (1) the inhibition of reseeding of cancer cells beside HT-29 colon cancer cells (2) reseeding prior to surgical resection of a tumor and (3) the genus of the compounds of claim 1, with at least a reasonable expectation of successfully achieving the treatment of the same. The instant

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specification fails to present any evidence, either in the form of data or scientifically sound reasoning, which would provide such a reasonable expectation that the claimed compounds would have been effective for the inhibition of reseeding of cancer cells. Though it is noted that Applicant need not necessarily demonstrate the precise manner in which the claimed therapeutic agent(s) ameliorate a particular disease state, such a mechanism must be elucidated in cases where Applicant relies upon a correlation between the particular activity of a compound and a reasonable expectation of efficacy in treating a particular disease.

The relevant examples provided by Applicant are drawn to the seeding of colon cancer cells with administration of BAY 11-7085 prior to surgical resection. Specifically, the example used two cell lines HCT-116 and HT-29. As stated in the specification, after 21 days there was clear evidence of metastases involving the parietal and visceral peritoneum of the mice injected with HTC-116 cells regardless of whether they did or did not receive BAY 11-7085. In contrast, mice injected intraabdominally with HT-29 and treated with BAY 11-7085 did not show evidence of hepatic metastases (page 68 of the instant specification).

In light of the fact that the specification not only fails to provide the skilled artisan with any direction or guidance as to how the treatment of any other cancer cell or tumor type, aside from HT-29 colon cancer, could actually be achieved using the claimed combination, but also fails to direct the skilled artisan as to which other tumor types would be sensitive to this chemotherapeutic agent and how one would determine such sensitivity, the specification, which lacks an objective showing of which other tumors could be effectively treated using the claimed combination, is viewed as lacking an enabling disclosure of the entire scope of the claimed invention, especially in light of the highly complex nature of tumors and cancer in general.

Here, the objective truth that any tumor type may be treated with the claimed compound is doubted because, while the state of the prior art of cancer treatment is well developed with regard to the

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treatment of specific cancer types with specific chemotherapeutic regiment (see Cecil's Textbook of Medicine, pages 1060-1074), the state of the art with regard to treating all tumors using a single agent is grossly underdeveloped.

In this regard, Cecil's Textbook of Medicine (2000) is cited. In particular, there is no known anticancer agent or combination of anticancer agents that is effective against treating all cancer types, nor is there any known anticancer agent or combination of agents that is effective against inhibiting the growth of any type of cancer cell. The Cecil reference clearly shows that for the various known cancer types, there is not one specific chemotherapeutic agent or combination thereof that is effective at treating cancer or inhibiting the growth of cancer cells for each and every type of cancer (see Table 198-5 at page 1065; Tables 198-6 and 198-7 at pages 1066; Table 198-8 at page 1068; and Table 198-9 at page 1071).

Given that there was not known any specific agent or combination of agents effective to treat all known type of cancer cells or tumors, one of ordinary skill in the art would not accept on its face Applicant's statement that such an objective could be achieved in any type of cancer cell or tumor using the presently claimed compound without enabling a set of species representative of full scope of cancers known in the art. The artisan would have required sufficient direction as to how, at minimum, a representative set of species for cancer could be effectively treated with the compound and, further, how the artisan could have reasonably extrapolated such results to the larger and highly varied genus of cancer cells and/or tumors in general would actually show sensitivity to the presently claimed compound, such that the artisan would have been imbued with at least a reasonable expectation of success in treating the cancer. Such success would not have been reasonably expected for all cancer cell and/or tumor types claimed given the highly complex and variable nature of all cancers known in the art and that Applicant has shown examples only in colon cancer cells. To the artisan, the concept of a single agent effect to treat this subset of cancer types would not have been considered representative or suggestive of the same efficacy in the treatment of all known types of cancer cells and/or tumors in the absence of any evidence

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or reasoning to do so. Additionally, since the skilled artisan would have expected in the interaction of a particular agent in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for the use of each agent, one of skill in the art would have no other recourse but undue experimentation to undertake extensive testing to determine which other cancer cell and/or tumor types would be amenable to treatment using the claimed compound.

The prior art teaches that BAY 11-7085 is known for its anti-inflammatory activity (Lawrence et al; Nature Medicine, (7):12, 2001; see Figure 3).

Notably, the purported effect and/or specific interaction of the (1) the inhibition of reseeding of cancer cells beside colon cancer (2) the inhibition prior to resection and (3) the inhibition by the genus of compounds of claim 1, is never described within the four corners of the instant specification. The specification fails to present either view a working or prophetic example(s) or a clear, scientifically sound explanation as to what, in fact, enables the above, such that the skilled artisan would have been imbued with at least a reasonable expectation of predictability of action in using the instantly claimed compound for use in treating any one or more of the disorders disclosed as being responsive to such an effect.

Absent such guidance, the experimentation required, without needing to resort to random speculation, what therapeutic amounts would be available to even start testing for a therapeutic effect, would clearly be undue. Further, it is noted that, while the lack of a working embodiment cannot be the *sole* factor in determining enablement, the absence of substantial evidence commensurate in scope with the breadth of the presently claimed subject matter, in light of the unpredictable nature of the chemical and pharmaceutical arts and the limited direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

As stated in MPEP §2164.04[R-1], "Doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could

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not develop without undue experimentation." In the absence of this information, the specification fails to provide adequate guidance and/or direction to one of skill in the art at the time of the invention that would have enabled such a person to practice the instantly claimed invention without having to resort to undue experimentation to determine how, in fact, one would achieve the instantly disclosed therapeutic objective(s).

The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the prior art and Applicant's disclosure and remarks that experimentation in this particular art is not at all uncommon, but that the experimentation required in order to practice the full scope of the invention would be *undue*. Please reference *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*." (emphasis added) Accordingly, in the absence of any adequate disclosure, direction or guidance as to how one would go about using the instantly claimed compound with a reasonable expectation of successfully treating the disclosed disorder(s), it remains that the pharmaceutical, chemical and medical arts are notoriously complex such that methods of use would have been sufficiently unpredictable to warrant the need for undue experimentation to actually practice the full scope of the invention as instantly claimed.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of a medical doctor or scientist with several years of experience in the art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation or ability to make and use the full scope of the invention as instantly claimed, given the disclosure and supporting examples provided in the present specification and the state of the art at the time of the invention. In order to actually achieve the claimed invention, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph,

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and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the embodiments presently claimed.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP
/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642